From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark Office
Box PCT
Washington, D.C.20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 06 December 1999 (06.12.99)	
International application No. PCT/EP99/03038	**Applicant's or agent's file reference** FB/BM45311
International filing date (day/month/year) 03 May 1999 (03.05.99)	**Priority date** (day/month/year) 06 May 1998 (06.05.98)
Applicant RUELLE, Jean-Louis	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

08 November 1999 (08.11.99)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Catherine Massetti
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

CLAIMS:

1. An isolated polypeptide comprising an amino acid sequence which has at least 85% identity to the amino acid sequence selected from the group consisting of: SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 and SEQ ID NO:8.

2. An isolated polypeptide as claimed in claim 1 in which the amino acid sequence has at least 95% identity to the amino acid sequence selected from the group consisting of: SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 and SEQ ID NO:8.

3. The polypeptide as claimed in claim 1 comprising the amino acid sequence selected from the group consisting of: SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 and SEQ ID NO:8.

4. An isolated polypeptide of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 and SEQ ID NO:8.

5. An immunogenic fragment of the polypeptide as claimed in any one of claims 1 to 4 in which the immunogenic activity of said immunogenic fragment is substantially the same as the polypeptide of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 or SEQ ID NO:8.

6. An isolated polynucleotide comprising a nucleotide sequence encoding a polypeptide that has at least 85% identity to the amino acid sequence of SEQ ID NO:2, 4 6 or 8 over the entire length of SEQ ID NO:2, 4, 6 or 8 respectively; or a nucleotide sequence complementary to said isolated polynucleotide.

7. An isolated polynucleotide comprising a nucleotide sequence that has at least 85% identity to a nucleotide sequence encoding a polypeptide of SEQ ID NO:2, 4, 6 or 8 over the

entire coding region; or a nucleotide sequence complementary to said isolated polynucleotide.

8. An isolated polynucleotide which comprises a nucleotide sequence which has at least 85% identity to that of SEQ ID NO:1, 3, 5 or 7 over the entire length of SEQ ID NO:1, 3, 5 or 7 respectively; or a nucleotide sequence complementary to said isolated polynucleotide.

9. The isolated polynucleotide as claimed in any one of claims 6 to 8 in which the identity is at least 95% to SEQ ID NO:1, 3, 5 or 7.

10. An isolated polynucleotide comprising a nucleotide sequence encoding the polypeptide of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 or SEQ ID NO:8.

11. An isolated polynucleotide comprising the polynucleotide of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5 or SEQ ID NO:7.

12. An isolated polynucleotide comprising a nucleotide sequence encoding the polypeptide of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 or SEQ ID NO:8, obtainable by screening an appropriate library under stringent hybridization conditions with a labeled probe having the sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5 or SEQ ID NO:7 or a fragment thereof.

13. An expression vector or a recombinant live microorganism comprising an isolated polynucleotide according to any one of claims 6 - 12.

14. A host cell comprising the expression vector of claim 13 or a membrane of said host cell expressing an isolated polypeptide comprising an amino acid sequence that has at

least 85% identity to the amino acid sequence selected from the group consisting of: SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 or SEQ ID NO:8.

15. A process for producing a polypeptide comprising an amino acid sequence that has at least 85% identity to the amino acid sequence selected from the group consisting of: SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 or SEQ ID NO:8 comprising culturing a host cell of claim 14 under conditions sufficient for the production of said polypeptide and recovering the polypeptide from the culture medium.

16. A process for expressing a polynucleotide of any one of claims 6 – 12 comprising transforming a host cell with the expression vector comprising at least one of said polynucleotides and culturing said host cell under conditions sufficient for expression of any one of said polynucleotides.

17. A vaccine composition comprising an effective amount of the polypeptide of any one of claims 1 to 5 and a pharmaceutically acceptable carrier.

18. A vaccine composition comprising an effective amount of the polynucleotide of any one of claims 6 to 12 and a pharmaceutically effective carrier.

19. The vaccine composition according to either one of claims 17 or 18 wherein said composition comprises at least one other *Moraxella catarrhalis* antigen.

20. An antibody immunospecific for the polypeptide or immunological fragment as claimed in any one of claims 1 to 5.

21. A method of diagnosing a Moraxella infection, comprising identifying a polypeptide as claimed in any one of claims 1 - 5, or an antibody that is immunospecific for said

polypeptide, present within a biological sample from an animal suspected of having such an infection.

22. Use of a composition comprising an immunologically effective amount of a polypeptide as claimed in any one of claims 1 – 5 in the preparation of a medicament for use in generating an immune repsonse in an animal.

23. Use of a composition comprising an immunologically effective amount of a polynucleotide as claimed in any one of claims 6 - 12 in the preparation of a medicament for use in generating an immune repsonse in an animal.

24. A therapeutic composition useful in treating humans with *Moraxella catarrhalis* disease comprising at least one antibody directed against the polypeptide of claims 1 – 5 and a suitable pharmaceutical carrier.

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PATENT COOPERATION TREATY

REC'D 18 AUG 2000

WIPO PCT

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
FB/BM45311		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP99/03038	03/05/1999	06/05/1998
International Patent Classification (IPC) or national classification and IPC		
C12N15/31		
Applicant		
SMITHKLINE BEECHAM BIOLOGICALS S.A. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 4 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☒ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
08/11/1999	14.08.00
Name and mailing address of the international preliminary examining authority:	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Fotaki, M Telephone No. +49 89 2399 8709

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP99/03038

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-72 as originally filed

Claims, No.:

1-26 as received on 20/07/2000 with letter of 18/07/2000

Drawings, sheets:

1/13-13/13 as originally filed

2. The amendments have resulted in the cancellation of:

☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-14, 16-21, 23-26
	No:	Claims	15, 22
Inventive step (IS)	Yes:	Claims	1-14, 16-18, 23
	No:	Claims	15, 19-22, 24-26
Industrial applicability (IA)	Yes:	Claims	1-26
	No:	Claims	

2. Citations and explanations

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

V. REASONED STATEMENT UNDER ARTICLE 35(2).

1) The present application relates to the identification of a polypeptide originating from Moraxella catarrhalis, called BASB019, represented by four polypeptide sequences related by 97% identity, SEQ ID NO 2, 4, 6, 8. The BASB019 polypeptide showed a 43% identity with the peptidoglycan associated outer membrane lipoprotein (PAL) of Pseudomonas putida. The cloned polypeptide was expressed recombinantly and used to generate antisera in rabbits. The antisera recognized a 17-18 kDa protein in all Moraxella strains. An antibody recognized by BASB019 is detected in human sera of infected individuals. The use of BASB019 polypeptide is applicable in diagnostic methods. Its use in a vaccine for preventing or eliminating infection has not been demonstrated.

2) The prior art documents:
D1: MURPHY T F: 'Branhamella catarrhalis: epidemiology, surface antigenic structure, and immune response.' MICROBIOL. REVIEWS, vol. 60, no. 2, June 1996 (1996-06), pages 267-279;
D2: BARTOS L C ET AL: 'Comparison of the outer membranae proteins of 50 strains of Branhamella catarrhalis.' JOURNAL OF INFECTIOUS DISEASES, vol. 158, no. 4, October 1988 (1988-10), page 761-765 ;
D3: WO 95 31215 A (UNIV NEW YORK) 23 November 1995 (1995-11-23), cited in the International Search Report disclose proteins of the outer membrane originating from Moraxella catarrhalis. However, a polypeptide with the molecular weight or the amino acid sequence of the BASB019 polypeptide has not been disclosed or rendered obvious by said documents.

The documents of the prior art :
D4: LIM A JR ET AL.: 'Molecular and immunological characterization of OprL, the 18 kDa outer-membrane peptidoglycan-associated lipoprotein (PAL) of Pseudomonas aeruginosa.' MICROBIOLOGY, vol. 143, no. 5, May 1997 (1997-05), pages 1709-1716;
D5: EP-A-0 281 673 (UNIV NEW YORK) 14 September 1988 (1988-09-14);
D6: SPINOLA S M ET AL.: 'The conserved 18,000-molecular-weight outer membrane protein of Haemophilus ducreyi has homology to PAL.' INFECTION AND IMMUNITY, vol. 64, no. 6, June 1996 (1996-06), pages 1950-1955;

D7: SPINOLA S M ET AL.: 'Characterization of an 18,000-molecular-weight outer membrane protein of Haemophilus ducreyi that contains a conserved surface-exposed epitope.' INFECTION AND IMMUNITY, vol. 60, no. 2, February 1992 (1992-02), pages 385-391,
disclose an 18 kDa outer membrane protein originating from Pseudomonas aeruginosa, Haemophilus ducreyi or H. influenza, showing a 40-49% identity with the BASB019 polypeptide. However, these documents do not disclose nor render obvious the isolation of the homologous protein from Moraxella catarrhalis. Thus, in light of the cited prior art, the subject-matter of **Claims 1-14, 16-18, 23** is novel and inventive as required by Article 33(3) PCT.

3) The subject-matter of **Claim 22** is not novel as required by Article 33(2) PCT.

Said claim relates to an antibody immunospecific for the polypeptide as claimed in any one of **Claims 1-6**. Said polypeptide is only partially defined by means of comprising an amino acid sequence related to BASB019. However, it remains undefined as to what other sequences may be present in the polypeptide as claimed. These undefined sequences include already known sequences, for example, known immunogenic sequences. So-defined, the subject-matter of **Claim 22** includes antibodies specific for any sequence which may be present in the polypeptide as claimed in any one of **Claims 1-6**, including known antibodies recognizing known immunogenic sequences. Thus, said subject-matter is not novel.

4) The subject-matter of **Claim 15** is not novel as required by Article 33(2) PCT.

Said claim relates to a recombinant live microorganism comprising an isolated polynucleotide according to any one of **claims 7-14**. The claimed microorganism is indistinguishable from the naturally occurring Moraxella strain where the BASB019 polypeptide was isolated from and thus, not novel.

The argument that the claimed microorganism is produced recombinantly and thus, novel over the naturally occurring Moraxella strain, is not taking into account the fact that the method of production of said microorganism does not impart any distinguishing technical feature to the microorganism. In other words, the claimed

recombinantly produced microorganism comprising said polynucleotide has technical features identical to those of the naturally occurring Moraxella strain.

5) The subject-matter of **Claims 19-21, 24-26** is not inventive as required by Article 33(3) PCT.

Said claims relate to subject-matter for which no demonstrated function is disclosed in the application as filed. It is speculated that BASB019 would be useful in prevention and treatment of such microbial diseases as a vaccine or as a therapeutic composition (p. 4, 5, 33, 40). Since there is no conclusive demonstration of any of these presumed properties of the BASB019 polypeptide, a protective function against microbial infections can only be accepted as speculative. Therefore, it is not clear whether or not the claimed vaccine compositions and therapeutic compositions would solve the posed problem which will be the identification of a composition capable of protective or therapeutic function against Moraxella infection. Consequently, the acknowledgement of an inventive step involved in solving said technical problem is impossible.

VII. CERTAIN DEFECTS IN THE INTERNATIONAL APPLICATION

6) The following discrepancy exists in the description as filed: On page 70 it is mentioned that "western blots of purified recombinant BASB019, using anti-peptide antibodies as the first antibody, were prepared as described in Example 4 and 6. The results are presented in Figure 8". However, Figure 8 shows a "western blot of purified recombinant BASB019 protein probed with pooled human convalescent sera at 1:100" and not probed with anti-peptide antibodies.

VIII. CERTAIN OBSERVATIONS ON THE INTERNATIONAL APPLICATION

7) **Claim 1** is drafted towards an isolated polypeptide with broadly specified sequence content as comprising an amino acid sequence which has at least 85% identity to the amino acid sequence of any of SEQ ID NO 2, 4 or 6. The Applicant indicates in the description that said polypeptide, (BASB019), as it relates to a polypeptide originating from Moraxella catarrhalis, it is suitable for diagnosis of a disease associated with said microorganism. However, the function of said

polypeptide is not clearly stated in the claim. The Applicant is reminded that the function of a newly identified protein or nucleic acid is prerequisite to the final assessment of inventive step and industrial applicability before a patent may be granted.

The same deficiency is present in the subject-matter of **Claims 2-4, 6-16.**

8) As mentioned above in section (5), there is no conclusive demonstration of any protective or therapeutic function of the BASB019 polypeptide or an antibody directed against said polypeptide. Therefore, the subject-matter of **Claims 19-21, 24-26** is not supported by the description as required by Article 6 PCT. The application as filed does not demonstrate clearly and unambiguously that a composition comprising a BASB019 polypeptide or an antibody directed against the BASB019 polypeptide would be therapeutic and useful as medicament in treating humans with Moraxella catarrhalis disease.

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

KATHRYN LOUISE PRIVETT
SMITHKLINE BEECHAM
Corporate Intellectual Property
Two New Horizons Court
Brentford
Middlesex TW8 9EP
GRANDE BRETAGNE

RECEIVED
18 AUG 2000
NEW HORIZONS COURT

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Rule 71.1)

	Date of mailing *(day/month/year)* 14. 08. 00
Applicant's or agent's file reference FB/BM45311	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP99/03038	03/05/1999	06/05/1998

Applicant
SMITHKLINE BEECHAM BIOLOGICALS S.A. et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Vullo, C Tel.+49 89 2399-8061

Form PCT/IPEA/416 (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
FB/BM45311		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP99/03038	03/05/1999	06/05/1998
International Patent Classification (IPC) or national classification and IPC C12N15/31		
Applicant SMITHKLINE BEECHAM BIOLOGICALS S.A. et al.		

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   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
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   - VII ☒ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
08/11/1999	14.08.00
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Fotaki, M Telephone No. +49 89 2399 8709

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP99/03038

I. Basis of the report

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Description, pages:

1-72	as originally filed				

Claims, No.:

1-26	as received on	20/07/2000	with letter of	18/07/2000	

Drawings, sheets:

1/13-13/13	as originally filed

2. The amendments have resulted in the cancellation of:

☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-14, 16-21, 23-26
	No:	Claims	15, 22
Inventive step (IS)	Yes:	Claims	1-14, 16-18, 23
	No:	Claims	15, 19-22, 24-26
Industrial applicability (IA)	Yes:	Claims	1-26
	No:	Claims	

2. Citations and explanations

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

V. REASONED STATEMENT UNDER ARTICLE 35(2).

1) The present application relates to the identification of a polypeptide originating from Moraxella catarrhalis, called BASB019, represented by four polypeptide sequences related by 97% identity, SEQ ID NO 2, 4, 6, 8. The BASB019 polypeptide showed a 43% identity with the peptidoglycan associated outer membrane lipoprotein (PAL) of Pseudomonas putida. The cloned polypeptide was expressed recombinantly and used to generate antisera in rabbits. The antisera recognized a 17-18 kDa protein in all Moraxella strains. An antibody recognized by BASB019 is detected in human sera of infected individuals. The use of BASB019 polypeptide is applicable in diagnostic methods. Its use in a vaccine for preventing or eliminating infection has not been demonstrated.

2) The prior art documents:
D1: MURPHY T F: 'Branhamella catarrhalis: epidemiology, surface antigenic structure, and immune response.' MICROBIOL. REVIEWS, vol. 60, no. 2, June 1996 (1996-06), pages 267-279;
D2: BARTOS L C ET AL: 'Comparison of the outer membranae proteins of 50 strains of Branhamella catarrhalis.' JOURNAL OF INFECTIOUS DISEASES, vol. 158, no. 4, October 1988 (1988-10), page 761-765 ;
D3: WO 95 31215 A (UNIV NEW YORK) 23 November 1995 (1995-11-23), cited in the International Search Report disclose proteins of the outer membrane originating from Moraxella catarrhalis. However, a polypeptide with the molecular weight or the amino acid sequence of the BASB019 polypeptide has not been disclosed or rendered obvious by said documents.

The documents of the prior art :
D4: LIM A JR ET AL.: 'Molecular and immunological characterization of OprL, the 18 kDa outer-membrane peptidoglycan-associated lipoprotein (PAL) of Pseudomonas aeruginosa.' MICROBIOLOGY, vol. 143, no. 5, May 1997 (1997-05), pages 1709-1716;
D5: EP-A-0 281 673 (UNIV NEW YORK) 14 September 1988 (1988-09-14);
D6: SPINOLA S M ET AL.: 'The conserved 18,000-molecular-weight outer membrane protein of Haemophilus ducreyi has homology to PAL.' INFECTION AND IMMUNITY, vol. 64, no. 6, June 1996 (1996-06), pages 1950-1955;

D7: SPINOLA S M ET AL.: 'Characterization of an 18,000-molecular-weight outer membrane protein of Haemophilus ducreyi that contains a conserved surface-exposed epitope.' INFECTION AND IMMUNITY, vol. 60, no. 2, February 1992 (1992-02), pages 385-391,
disclose an 18 kDa outer membrane protein originating from Pseudomonas aeruginosa, Haemophilus ducreyi or H. influenza, showing a 40-49% identity with the BASB019 polypeptide. However, these documents do not disclose nor render obvious the isolation of the homologous protein from Moraxella catarrhalis. Thus, in light of the cited prior art, the subject-matter of **Claims 1-14, 16-18, 23** is novel and inventive as required by Article 33(3) PCT.

3) The subject-matter of **Claim 22** is not novel as required by Article 33(2) PCT.

Said claim relates to an antibody immunospecific for the polypeptide as claimed in any one of **Claims 1-6**. Said polypeptide is only partially defined by means of comprising an amino acid sequence related to BASB019. However, it remains undefined as to what other sequences may be present in the polypeptide as claimed. These undefined sequences include already known sequences, for example, known immunogenic sequences. So-defined, the subject-matter of **Claim 22** includes antibodies specific for any sequence which may be present in the polypeptide as claimed in any one of **Claims 1-6**, including known antibodies recognizing known immunogenic sequences. Thus, said subject-matter is not novel.

4) The subject-matter of **Claim 15** is not novel as required by Article 33(2) PCT.

Said claim relates to a recombinant live microorganism comprising an isolated polynucleotide according to any one of **claims 7-14**. The claimed microorganism is indistinguishable from the naturally occurring Moraxella strain where the BASB019 polypeptide was isolated from and thus, not novel.

The argument that the claimed microorganism is produced recombinantly and thus, novel over the naturally occurring Moraxella strain, is not taking into account the fact that the method of production of said microorganism does not impart any distinguishing technical feature to the microorganism. In other words, the claimed

recombinantly produced microorganism comprising said polynucleotide has technical features identical to those of the naturally occurring Moraxella strain.

5) The subject-matter of **Claims 19-21, 24-26** is not inventive as required by Article 33(3) PCT.

Said claims relate to subject-matter for which no demonstrated function is disclosed in the application as filed. It is speculated that BASB019 would be useful in prevention and treatment of such microbial diseases as a vaccine or as a therapeutic composition (p. 4, 5, 33, 40). Since there is no conclusive demonstration of any of these presumed properties of the BASB019 polypeptide, a protective function against microbial infections can only be accepted as speculative. Therefore, it is not clear whether or not the claimed vaccine compositions and therapeutic compositions would solve the posed problem which will be the identification of a composition capable of protective or therapeutic function against Moraxella infection. Consequently, the acknowledgement of an inventive step involved in solving said technical problem is impossible.

VII. CERTAIN DEFECTS IN THE INTERNATIONAL APPLICATION

6) The following discrepancy exists in the description as filed: On page 70 it is mentioned that "western blots of purified recombinant BASB019, using anti-peptide antibodies as the first antibody, were prepared as described in Example 4 and 6. The results are presented in Figure 8". However, Figure 8 shows a "western blot of purified recombinant BASB019 protein probed with pooled human convalescent sera at 1:100" and not probed with anti-peptide antibodies.

VIII. CERTAIN OBSERVATIONS ON THE INTERNATIONAL APPLICATION

7) **Claim 1** is drafted towards an isolated polypeptide with broadly specified sequence content as comprising an amino acid sequence which has at least 85% identity to the amino acid sequence of any of SEQ ID NO 2, 4 or 6. The Applicant indicates in the description that said polypeptide, (BASB019), as it relates to a polypeptide originating from Moraxella catarrhalis, it is suitable for diagnosis of a disease associated with said microorganism. However, the function of said

polypeptide is not clearly stated in the claim. The Applicant is reminded that the function of a newly identified protein or nucleic acid is prerequisite to the final assessment of inventive step and industrial applicability before a patent may be granted.

The same deficiency is present in the subject-matter of **Claims 2-4, 6-16.**

8) As mentioned above in section (5), there is no conclusive demonstration of any protective or therapeutic function of the BASB019 polypeptide or an antibody directed against said polypeptide. Therefore, the subject-matter of **Claims 19-21, 24-26** is not supported by the description as required by Article 6 PCT. The application as filed does not demonstrate clearly and unambiguously that a composition comprising a BASB019 polypeptide or an antibody directed against the BASB019 polypeptide would be therapeutic and useful as medicament in treating humans with Moraxella catarrhalis disease.

BM45311

CLAIMS:

1. An isolated immunogenic polypeptide comprising an amino acid sequence which has at least 85% identity to the amino acid sequence selected from the group consisting of: SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 and SEQ ID NO:8 over the entire length of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 or SEQ ID NO:8 respectively.

2. An isolated polypeptide as claimed in claim 1 in which the amino acid sequence has at least 95% identity to the amino acid sequence selected from the group consisting of: SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 and SEQ ID NO:8, over the entire length of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 or SEQ ID NO:8 respectively.

3. The polypeptide as claimed in claim 1 comprising the amino acid sequence selected from the group consisting of: SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 and SEQ ID NO:8.

4. An isolated polypeptide having the amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 and SEQ ID NO:8.

5. An immunogenic fragment of the polypeptide as claimed in any one of claims 1 to 4 in which the immunogenic fragment is capable of raising an immune response (if necessary when coupled to a carrier) which recognises the polypeptide of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 or SEQ ID NO:8.

6. A polypeptide as claimed in any of claims 1 to 5 wherein said polypeptide is part of a larger fusion protein.

7. An isolated polynucleotide encoding a polypeptide as claimed in any of claims 1 to 6.

8. An isolated polynucleotide comprising a nucleotide sequence encoding a polypeptide that has at least 85% identity to the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 or SEQ ID NO:8 over the entire length of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 or SEQ ID NO:8 respectively.

9. An isolated polynucleotide comprising a nucleotide sequence that has at least 85% identity to a nucleotide sequence encoding a polypeptide of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 or SEQ ID NO:8 over the entire coding region; or a nucleotide sequence complementary to said isolated polynucleotide.

10. An isolated polynucleotide which comprises a nucleotide sequence which has at least 85% identity to that of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5 or SEQ ID NO:7 over the entire length of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5 or SEQ ID NO:7 respectively; or a nucleotide sequence complementary to said isolated polynucleotide.

11. The isolated polynucleotide as claimed in any one of claims 7 to 10 in which the identity is at least 95% to SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5 or SEQ ID NO:7.

12. An isolated polynucleotide comprising a nucleotide sequence encoding the polypeptide of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 or SEQ ID NO:8.

13. An isolated polynucleotide comprising the polynucleotide of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5 or SEQ ID NO:7.

14. An isolated polynucleotide comprising a nucleotide sequence encoding the polypeptide of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 or SEQ ID NO:8, obtainable by screening an appropriate library under stringent hybridization conditions with a labeled probe having the sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5 or SEQ ID NO:7 or a fragment thereof.

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15. An expression vector or a recombinant live microorganism comprising an isolated polynucleotide according to any one of claims 7 - 14.

16. A host cell comprising the expression vector of claim 15 expressing an isolated polypeptide comprising an amino acid sequence that has at least 85% identity to the amino acid sequence selected from the group consisting of: SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 or SEQ ID NO:8, or a membrane of the host cell containing the expressed polypeptide.

17. A process for producing a polypeptide of claims 1 to 6 comprising culturing a host cell of claim 16 under conditions sufficient for the production of said polypeptide and recovering the polypeptide from the culture medium.

18. A process for expressing a polynucleotide of any one of claims 7 – 14 comprising transforming a host cell with the expression vector comprising at least one of said polynucleotides and culturing said host cell under conditions sufficient for expression of any one of said polynucleotides.

19. A vaccine composition comprising an effective amount of the polypeptide of any one of claims 1 to 6 and a pharmaceutically acceptable carrier.

20. A vaccine composition comprising an effective amount of the polynucleotide of any one of claims 7 to 14 and a pharmaceutically effective carrier.

21. The vaccine composition according to either one of claims 19 or 20 wherein said composition comprises at least one other *Moraxella catarrhalis* antigen.

22. An antibody immunospecific for the polypeptide or immunological fragment as claimed in any one of claims 1 to 6.

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23. A method of diagnosing a *Moraxella catarrhalis* infection, comprising identifying a polypeptide as claimed in any one of claims 1 - 6, or an antibody that is immunospecific for said polypeptide, present within a biological sample from an animal suspected of having such an infection.

24. Use of a composition comprising an immunologically effective amount of a polypeptide as claimed in any one of claims 1 – 6 in the preparation of a medicament for use in generating an immune response in an animal.

25. Use of a composition comprising an immunologically effective amount of a polynucleotide as claimed in any one of claims 7 - 14 in the preparation of a medicament for use in generating an immune response in an animal.

26. A therapeutic composition useful in treating humans with *Moraxella catarrhalis* disease comprising at least one antibody directed against the polypeptide of claims 1 – 6 and a suitable pharmaceutical carrier.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
FB/BM45311		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/EP 99/ 03038	03/05/1999	06/05/1998
Applicant		
SMITHKLINE BEECHAM BIOLOGICALS S.A. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [X] contained in the international application in written form.

   [X] filed together with the international application in computer readable form.

   [ ] furnished subsequently to this Authority in written form.

   [ ] furnished subsequently to this Authority in computer readble form.

   [X] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [X] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

   [ ] the text is approved as submitted by the applicant.

   [X] the text has been established by this Authority to read as follows:

   BASB019 PROTEINS AND GENES FROM MARAXELLA CATARRHALIS, ANTIGENS, ANTIBODIES AND USES

5. With regard to the **abstract,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. 4

   [ ] as suggested by the applicant.

   [X] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

   [ ] None of the figures.

INTERNATIONAL SEARCH REPORT

[redacted]ional Application No
PCT/EP 99/03038

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/31 C12N15/62 C07K14/21 C07K16/12 A61K39/02
A61K39/40 G01N33/50

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C12N C07K A61K G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	MURPHY T F: "Branhamella catarrhalis: epidemiology, surface antigenic structure, and immune response." MICROBIOL. REVIEWS, vol. 60, no. 2, June 1996 (1996-06), pages 267-279, XP000857203 cited in the application page 271, right-hand column, paragraph 5 -page 273, right-hand column, paragraph 3 table 3 page 274, right-hand column, paragraph 2 -page 275, right-hand column, paragraph 3 --- -/--	1-24

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
1 December 1999	15/12/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	van de Kamp, M

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Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	BARTOS L C ET AL: "Comparison of the outer membrnae proteins of 50 strains of Branhamella catarrhalis." JOURNAL OF INFECTIOUS DISEASES, vol. 158, no. 4, October 1988 (1988-10), page 761-765 XP000562830 ISSN: 0022-1899 abstract figures 1,2 table 1 ---	1-24
A	LIM A JR ET AL.: "Molecular and immunological characterization of OprL, the 18 kDa outer-membrane peptidoglycan-associated lipoprotein (PAL) of Pseudomonas aeruginosa." MICROBIOLOGY, vol. 143, no. 5, May 1997 (1997-05), pages 1709-1716, XP000857202 Note: 40.3% aa sequence identity with SEQ ID NO:2 in 176 aa overlap. abstract figure 3 page 1713, paragraphs 2,3 page 1714, paragraphs 4,5 ---	1-24
A	EP 0 281 673 A (UNIV NEW YORK) 14 September 1988 (1988-09-14) Note: 49.5% aa sequence identity with SEQ ID NO:2 in 103 aa overlap. the whole document page 8 ---	1-24
A	SPINOLA S M ET AL.: "The conserved 18,000-molecular-weight outer membrane protein of Haemophilus ducreyi has homology to PAL." INFECTION AND IMMUNITY, vol. 64, no. 6, June 1996 (1996-06), pages 1950-1955, XP002124313 Note: 47.6% aa sequence identity with SEQ ID NO:2 in 103 aa overlap. abstract page 1950, paragraphs 3,4 figures 2,4 page 1954, paragraphs 1,3 ---	1-24

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	SPINOLA S M ET AL.: "Characterization of an 18,000-molecular-weight outer membrane protein of Haemophilus ducreyi that contains a conserved surface-exposed epitope." INFECTION AND IMMUNITY, vol. 60, no. 2, February 1992 (1992-02), pages 385-391, XP002124314 abstract page 387, line 12-20 ---	20
A	WO 95 31215 A (UNIV NEW YORK) 23 November 1995 (1995-11-23) the whole document -----	1-24

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/EP 99/03038

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